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18. A method according to Claim 17 wherein said disease or disorder is selected from the group consisting of inflammatory arthritis, multiple sclerosis, allograft rejection, diabetes, inflammatory dermatoses, asthma and inflammatory bowel disease.

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19. A method according to Claim 18 wherein said inflammatory arthritis is selected from the group consisting of rheumatoid arthritis vasculitis and polydermatomyositis.

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20. A method according to Claim 19 wherein said inflammatory dermatoses are selected from the group consisting of psoriasis and dermatitis.

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21. A method for inhibiting, in a mammal, the binding of  $\alpha 4$  integrins to the ligands thereof, comprising administering to the mammal an effective amount of a compound according to Claim 16.

20 19  
22. A method according to Claim 21 wherein the  $\alpha 4$  integrins are selected from the group consisting of  $\alpha 4\beta 1$  and  $\alpha 4\beta 7$  integrins.--

### REMARKS

Reconsideration of the present application in view of the above amendments and following remarks is requested respectfully.

Claims 2 to 22 are pending. Claim 1 has been canceled in favor of new claim 16.

New claims 17 to 22 have been added.

The present Office Action includes rejections under Section 112, second paragraph, which are discussed in detail below.

**Discussion of the Rejections Under Section 112, second paragraph**

The Office Action includes various objections to the form of Applicants' claims accompanied by a statement that the claims are indefinite. It is submitted respectfully that one of ordinary skill in the art would have no difficulty in understanding the metes and bounds of Applicants' original claims and the terminology used therein as they are both clear and definite. Nevertheless, to facilitate prosecution, certain amendments have been made.

In this connection, the brackets in claim 1 have been deleted and replaced in new claim 16 with parentheses in accordance with the Examiner's suggestion. With respect to the assertion that line 23 in claim 1 begins with a bracket but does not end with a bracket, Applicants respectfully point out that the corresponding bracket occurs on line 34, at the end of the definition of  $R^a$  and  $R^a$ .

The use of the term "heteroarylene" in the definition of  $Ar^2$  has been objected to because, according to the Office Action, it is unclear which heteroatoms Applicants intended. The Office Action also asserts that within the definition of  $R^1$ , the use of the terms "heteroaliphatic," "cycloaliphatic," "polycyclo-aliphatic," "heterocycloaliphatic," and

"heteropolycycloaliphatic," are unclear as to how many rings are present, what ring sizes are intended, and the nature and number of heteroatoms. Although Applicants certainly disagree that these terms lack definiteness, to facilitate prosecution these terms have been amended and presented in new claim 16 as follows.

The term "heteroarylene" has been deleted from the definition of  $Ar^2$ . In the definition of  $R^1$ , the term "aliphatic" has been amended to include a  $C_{1-6}$  carbon range. Support for this amendment is provided, for example, on page 10, lines 2 to 5 of the specification. The term "heteroaliphatic" has been replaced by the term " $C_{1-6}$  heteroaliphatic group containing one, two, three or four heteroatoms or heteroarom-containing groups." Support for this amendment is provided, for example, on page 10, lines 7 to 10 of the specification. The term "cycloaliphatic" has been amended to include a  $C_{3-10}$  carbon range. Support for this amendment is provided, for example, on page 11, lines 5 to 9 of the specification. The term "heterocycloaliphatic" has been replaced by the term " $C_{3-10}$  heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups." Support for this amendment is provided on page 11, lines 11 to 16 of the specification. The term "polycycloaliphatic" has been amended to include a  $C_{7-10}$  carbon range. Support for this amendment is provided on page 11, lines 18 to 20 of the specification. The term "heteropolycycloaliphatic" has been replaced by the term " $C_{7-10}$  heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups." Support for this amendment is provided, for example, on page 11, lines 20 to 23 of the specification. The term "heteroaromatic" has been replaced by the term

"heteroaromatic group containing one, two, three or four heteroatoms or heteroaromatic groups."

Support for this amendment is provided, for example, on page 13, lines 8 to 10 and page 6, lines 15 to 18 of the specification. The amended claims are believed to be of a scope equivalent to the scope of the originally filed claims.

Thus, as amended herein, the claims contain information as to both the ring size and nature of the heteroatoms contained within the definition of  $R^1$ . With respect to the assertion that the number of rings is indefinite, it is submitted respectfully that, based on their context within formula (1), the number of groups would be clear to the skilled artisan. For instance, where  $R^1$  is defined in terms of  $NHCOR^3$ , where  $R^3$  is an optionally substituted aliphatic, heteroaliphatic, cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, or heteropolycycloaliphatic group, there is clearly only one  $R^3$  group.

The Office Action also asserts that variable  $R^3$  is defined in a circular fashion, *i.e.*, defined in terms of  $R^3$  itself. Applicants disagree respectfully and submit that the definition of  $R^3$  is proper as the entire definition of  $R^3$  is presented in parentheses. Accordingly, the closed parenthesis terminate the definition of  $R^3$  prior to, for example, the presentation of substituent  $NHC(O)OR^3$ . Thus, Applicants respectfully submit that it is  $R^1$ , and not  $R^3$ , that is defined in terms of  $R^3$ .

The use of the term "derivative" within the definition of R has also been objected to. Although Applicants certainly disagree that one of ordinary skill would not recognize what is meant by the term "carboxylic acid derivatives," the term has been amended to read "ester and

amide." Support for this amendment is provided, for example, on page 6, line 2, of the specification.

The Office Action also asserts that the term "optionally substituted" is not understood inasmuch as it is unclear what kinds of "aromatic," "heteroaromatic," "aliphatic" and "heteroaliphatic" groups are substituted. Applicants believe that this objection is overcome in view of the above amendments. As noted, the claims clearly define the identity of the substituted groups, and as such, Applicants respectfully submit that further explanation is unnecessary.

Claims 1 to 15 also stand rejected as being drawn to an improper Markush group because the compounds contain a "variable core." Applicants respectfully disagree with this rejection and submit that the claims, as originally presented to the Patent Office, define proper Markush groups. Nevertheless, to advance prosecution, Applicants have amended the claims in an effort to address the Examiner's concerns. Applicants have deleted the term "nitrogen-containing six-membered heteroarylene group" from the definition of  $Ar^2$ . In addition, the groups  $-CON(R^3)(R^{3a})$  and  $-CON(R^3)(R^{3a})$  have been deleted from the definition of  $R^1$ . Consequently, the compounds encompassed by the pending claims all contain a 3-amino-3-phenyl propanoic acid core:  $-NHCH(Ph)C(R^a)(R^a)CO_2H$ .

It will be recognized that the present invention lies in the provision of novel  $\beta$ -alanine derivatives possessing desirable biological activity. Applicants have provided fifty working examples, set forth, for example, on pages 38 to 54 of the specification, each of which contain this common 3-amino-3-phenylpropanoic acid core as defined in the present claims.

Moreover, Applicants teach that biological activity may be maintained despite varying substituents  $R^a$  and  $R^{a1}$  and varying  $Ar^1$  from aromatic to heteroaromatic<sup>2</sup>. Applicants have also demonstrated that several  $L^1$  variants may be equally well-tolerated.<sup>3</sup>

It is well-established that where a Markush expression is applied only to a portion of a chemical compound, the propriety of the grouping is determined by a consideration of the compound as a whole. M.P.E.P. §2173.05(h). In such a situation, the grouping does not depend on there being a community of properties in the members of the Markush expression. *Id.* Here, Applicants have identified that the 3-amino-3-phenyl propanoic acid residue as a common structural element, and as such, Markush groupings may be identified accordingly. Thus, Applicants request respectfully reconsideration of the Markush rejection.

The Office Action asserts that although  $L^1$  is defined as  $-CON(R^2)-$ , in the elected species substituent  $L^1$  should be  $-NHC(O)-$  and therefore the elected compound is not embraced by the generic formula (1). Applicants disagree respectfully and submit that reading both the elected species and the structure of formula (1) from left to right, the elected compound clearly falls within the scope of claim 1 wherein  $L^1$  is  $CON(R^2)$ .

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<sup>1</sup> See, for example, Example 17 set forth on page 45 of the specification.

<sup>2</sup> See, for example, Examples 23 and 24 found on page 48 of the specification and Examples 25 and 26 found on page 49 of the specification.

<sup>3</sup> See, for example, Example 50, found on page 50 of the specification.

In view of the above amendments and remarks, reconsideration and withdrawal of the rejection under Section 112, second paragraph, is requested respectfully.

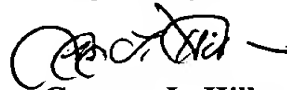
**Miscellaneous**

Applicants have added method claims 17 to 21. Support for these claims is provided, for example, on page 3, lines 25 to 31; page 21, line 33 to page 24, line 8; and page 54, line 31 to page 56, line 27 of the specification.

**Conclusion**

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the rejections and an allowance of the pending claims is requested respectfully.

Respectfully submitted,



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